

Fundamental Space Biology

during the early Space Station era

***Expanding opportunities for discoveries and applications
over the next five years***

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Fundamental Space Biology Vision

- Explore the biology of the only life that we know in its first generations beyond the home planet.
- Use the results to promote human expansion into space and benefits for Earth.
- Expand access to the biological frontier of space for discovery and education.

Fundamental Space Biology

Current Conditions

- Limited flight opportunities and flight constraints preclude implementing many experiments in the current flight queue.
 - *New opportunities are needed for a healthy discovery based program*
- Biotech/infotech/nanotech revolutions allow pioneering discoveries to be made in very small automated packages. These techniques open new biological discovery domains.
 - *Flight qualified hardware is on the shelf now to conduct these investigations.*

RECOMMENDATION: Bring back the Small Payloads Program to make new discoveries, increase flight opportunities, support human expeditions beyond LEO. *

* NRA selected investigations and ISSOLSWG agreements will always have priority.

Fundamental Space Biology

Small Payloads Project - 5 year Goals

- Fly experiments in the existing queue.
 - Deselect those that cannot be accommodated within a five year window.
- Conduct a focused baseline data collection program to establish the first set of biological reference standards for space.
 - Use model organisms that pioneered the Human Genome Project
 - Link gene expression changes at multiple time points in flight to their physical and biochemical causes and physiological consequences.
 - Use these reference organisms for radiation studies, centrifuge planetary gravity studies, as pioneers preceeding human expeditions beyond LEO, and as “canaries” during them.
- Establish a research quartet correlating human/rodent cell and tissue cultures of greatest interest to space medicine with whole animal effects in rodents and humans (collaboration with space medicine).
- Investigate areas of greatest promise for both fundamental knowledge and Earth applications.

What Is the FSB Small Payloads Project?

- Element of FSB Division
- Implementation to be led by FSB Program Office at ARC.
- Space flight and research support to be provided by ARC space life sciences organizations, technology development organizations, and information sciences organizations.
- Will contribute to baseline data needed for FSB Program goals, focus on model organisms and obtain data important to radiation biology and space medicine programs.
- Will use NASA approved solicitation and peer review mechanisms, some currently in use in FSB, others that were used in the past or are used in other NASA organizations.

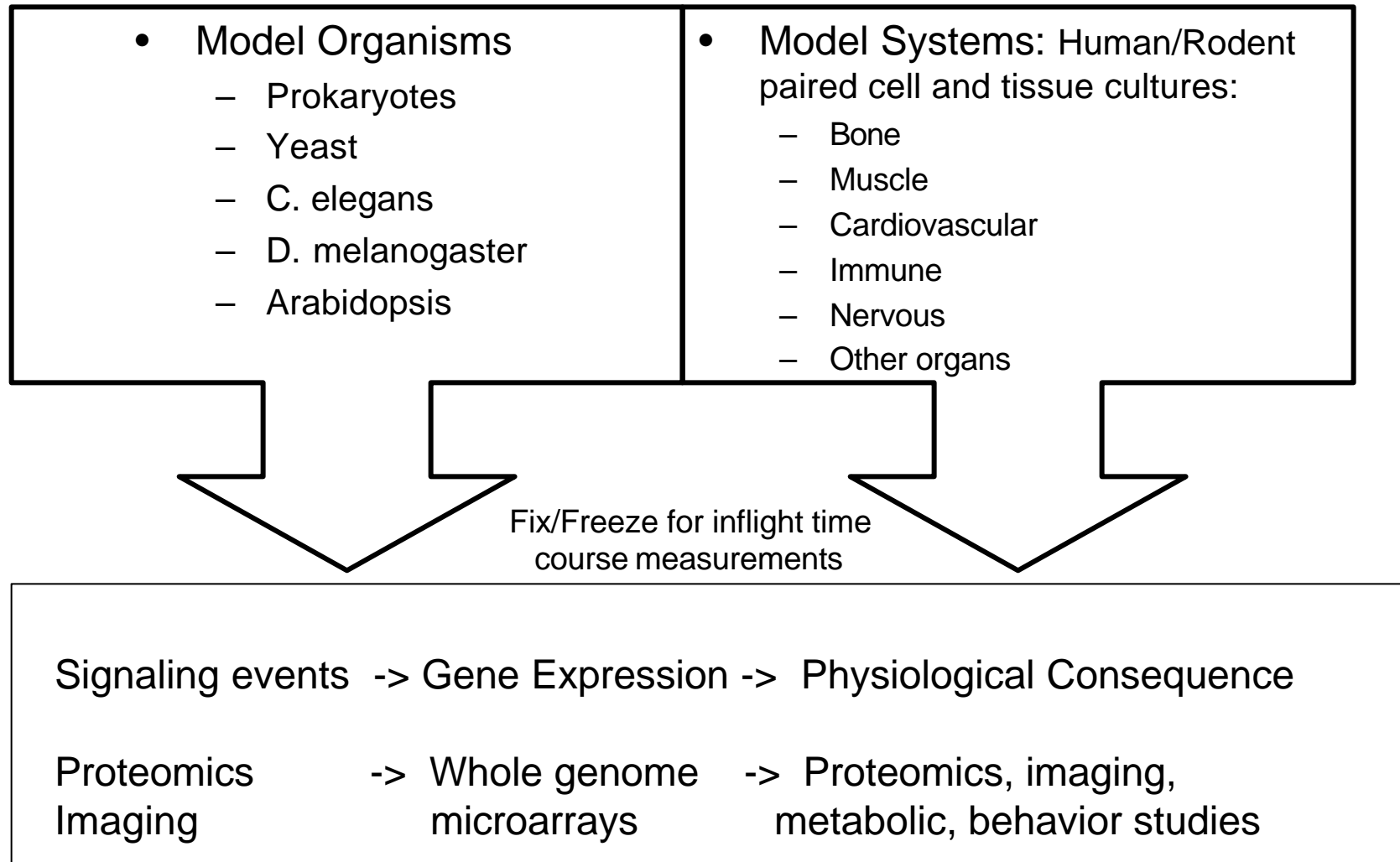
Fundamental Space Biology

Benefits of Small Payloads Project

Five Year Plan

- Open new discovery domains for biology even within near term constraints.
- Provide a historic first: Reference standards for space that link genomic responses to their causes and physiological consequences.
- Provide a unique NASA “wing” to the global library of genomically based reference standards on model organisms.
- Increase support for whole animal research in space.
- Amplify community access many fold, both by increased flight opportunities and data mining.
- Amplify yield of biological payloads.
- Establish new hands-on education programs.
- Develop new applications for public benefit.
- Support human expeditions beyond LEO by identifying root causes of space medical problems and new strategies for countermeasure development.
- Risk mitigation for flight hardware
- Confirmation of prior results
- Technology Testing

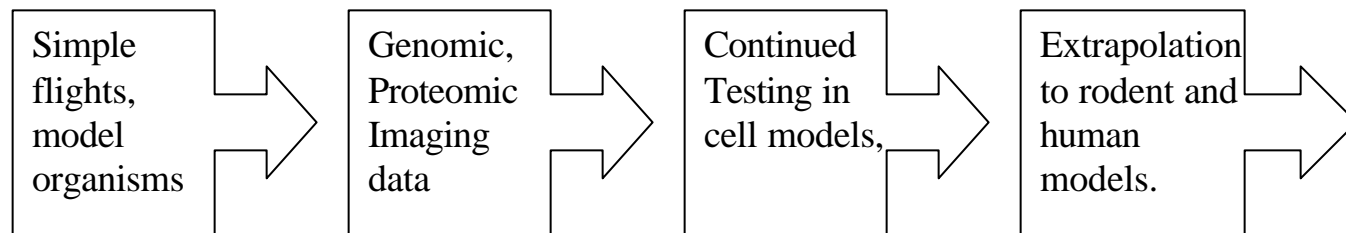
FSB: Small Payloads Project Science Outline



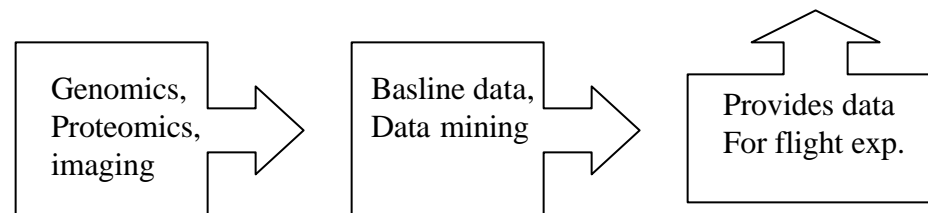
Science Solutions: cross disciplinary approach

- Concentrate on use of modern analytical techniques that provide information relevant across disciplines of space medicine, radiation biology, and fundamental biology
 - Genomics
 - Proteomics
 - Imaging analysis
- Use model organisms - Bacteria, mammalian cells, yeast, *Drosophila*, *C. elegans*, *Arabidopsis*.
 - Genome mapped, known models for studying general biological processes

- Flight: using existing hardware and constraints



- Ground: perform analysis in chosen hardware on the ground to provide baseline data for the hardware:



- *This program provides baseline data for ongoing and future gravitational biology studies in space medicine, radiation biology, and fundamental biology*

FSB: Small Payloads Project Implementation Mechanisms

Flight Strategies

- NOW:
 - Passive Velcro experiments
 - Piggybacks in powered and facility class instruments.
 - Dedicated middeck level equivalents
 - Free flyer payloads
- WITH TECHNOLOGY INVESTMENTS
 - New passive automated biological discovery systems suitable for any carrier.

Community Participation Strategies

- NOW:
 - Establish working groups
 - Initiate baseline data collection
 - Establish computational support
 - Focused DCL constrained to capabilities over next five years
 - Conduct flight verification tests
 - NRA for flight
 - NRA for data mining
 - NRA for graduate student fellowships
 - Support application programs

FSB: Small Payloads Project Feasibility

- Flight hardware immediately available for discovery piggybacks in powered equipment for all model organisms and cell/tissue models of interest as well as measurements of interest.
 - MOBIAS, CGBA, CCM, ADSEP, ARCTIC, MELFI, CRIM, STL-B, ADVASC
- Combination of BRIC + GN2 freezer + ESA PTCU enables velcro science in *C.elegans*, imbibed arabidopsis seeds, prokaryotes.
- Data archiving and bioinformatics scaffold already established at ARC. Team in place to support BDC, data mining, and 3/4D reconstruction.
- Sample bank already established at ARC.

FSB: Small Payloads Project

Technologies Needed

At the cell and molecular level, the quality of science discovery depends almost entirely on the quality of the technology applied to the discovery process.

Most urgent needs:

- **More sophisticated automated stand alone inflight growth and analysis systems** - to extend flights of opportunity to unpowered locations: lockers, payload bay, external Station, free flyers.
- **Snap freezer** - to enable on orbit initiation of experiments, extend shelf life of fixed samples, and preserve the biological “moment” in space for the widest range of postflight analyses.
- **Astronaut discovery kits** - Support the crew in making ad hoc investigations of issues critical for science discovery, risk mitigation, troubleshooting.
- **Imaging** - to obtain molecular level time lapse images to document the structural changes over time and evaluate organism/environment interface issues. Also major outreach element.

FSB Science Roadmap

2003-2006

2007-2010

2011-2020

LEO Free-Flyers and Space Station

Bioexplorers

Exploration

Research

- Changes in gene expression in space
- Sequence of cell events underlying space adaptation
- Changes in cell/tissue structure and organelle and biomolecule distribution
- Ground radiation studies
- Digital model organisms

- Initial predictive models
- Correlate tissue level changes with whole animal effects
- Terrestrial applications
- LEO radiation studies with known sources
- SBRP science

- Reference standards for deep space radiation
- Biological dosimeters "canaries"
- Digital Human in space
- Biologically-based technologies

Commercial

NASA

Other

Biotech, Pharm.

Bioastron., IS,

ALS, Fund Bio

NSF, NIH

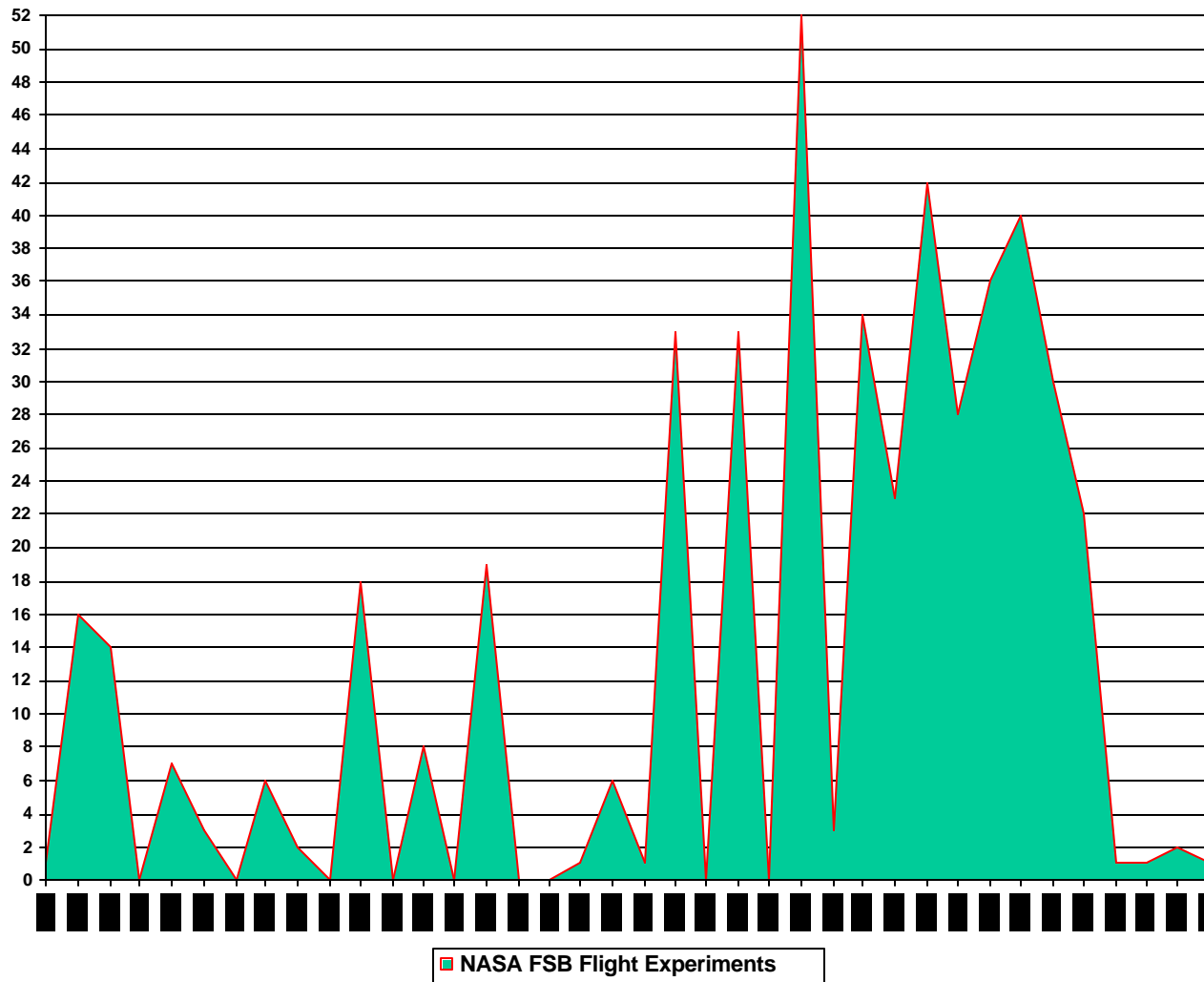
Academia



FSB Backup Slides

The Problem -- why its time to fly

NASA FSB Flight Experiments by Year 1965-2002



NOTE: This draft does not contain the KSC-sponsored FSB experiments for 1999-2002
Source: *Life into Space 1 and 2*; Ames Life Sciences Data Archive

FSB: Small Payloads Program

Why its time to fly

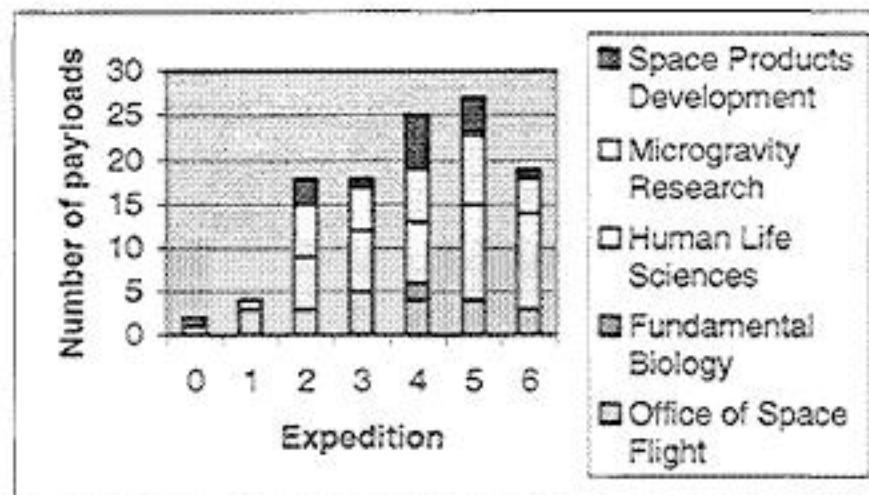
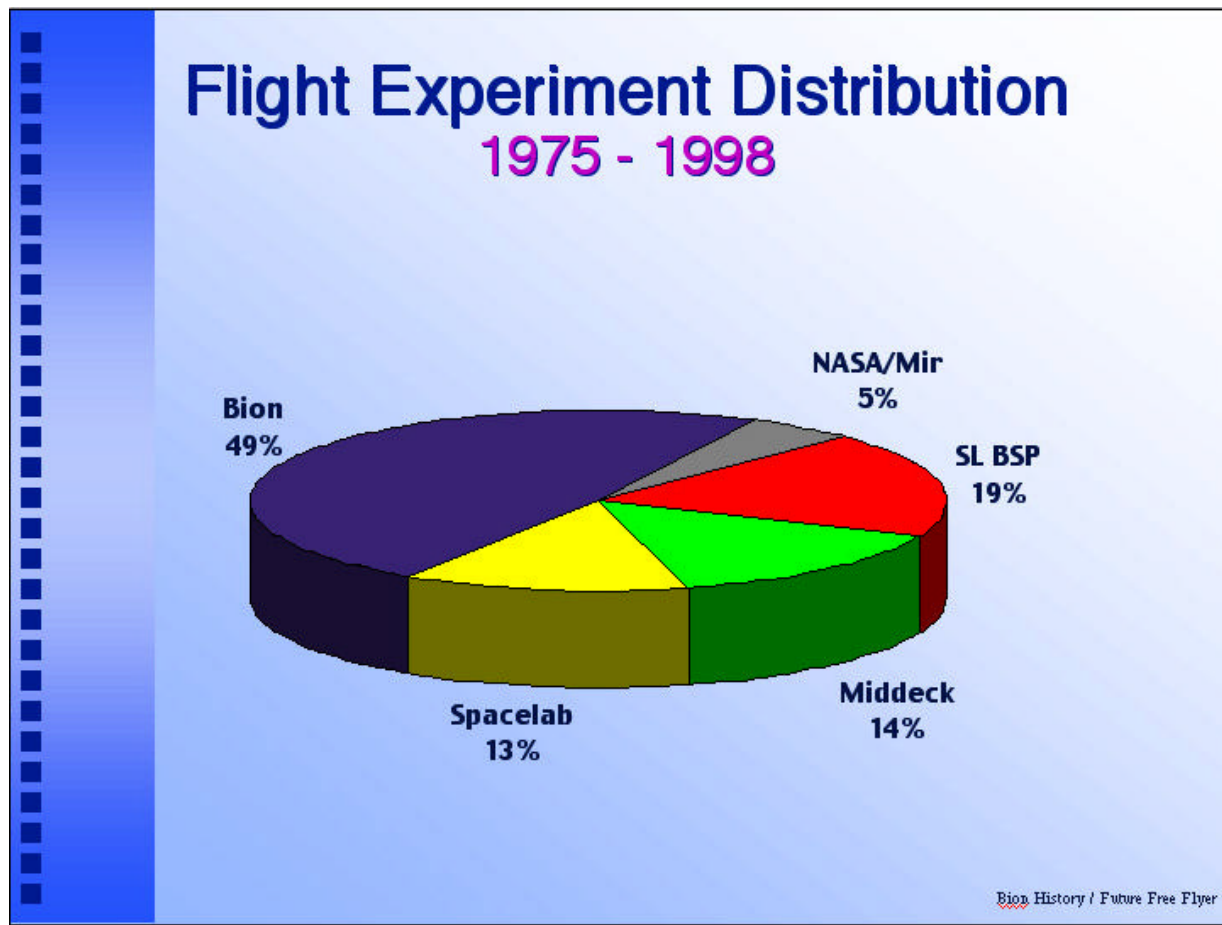
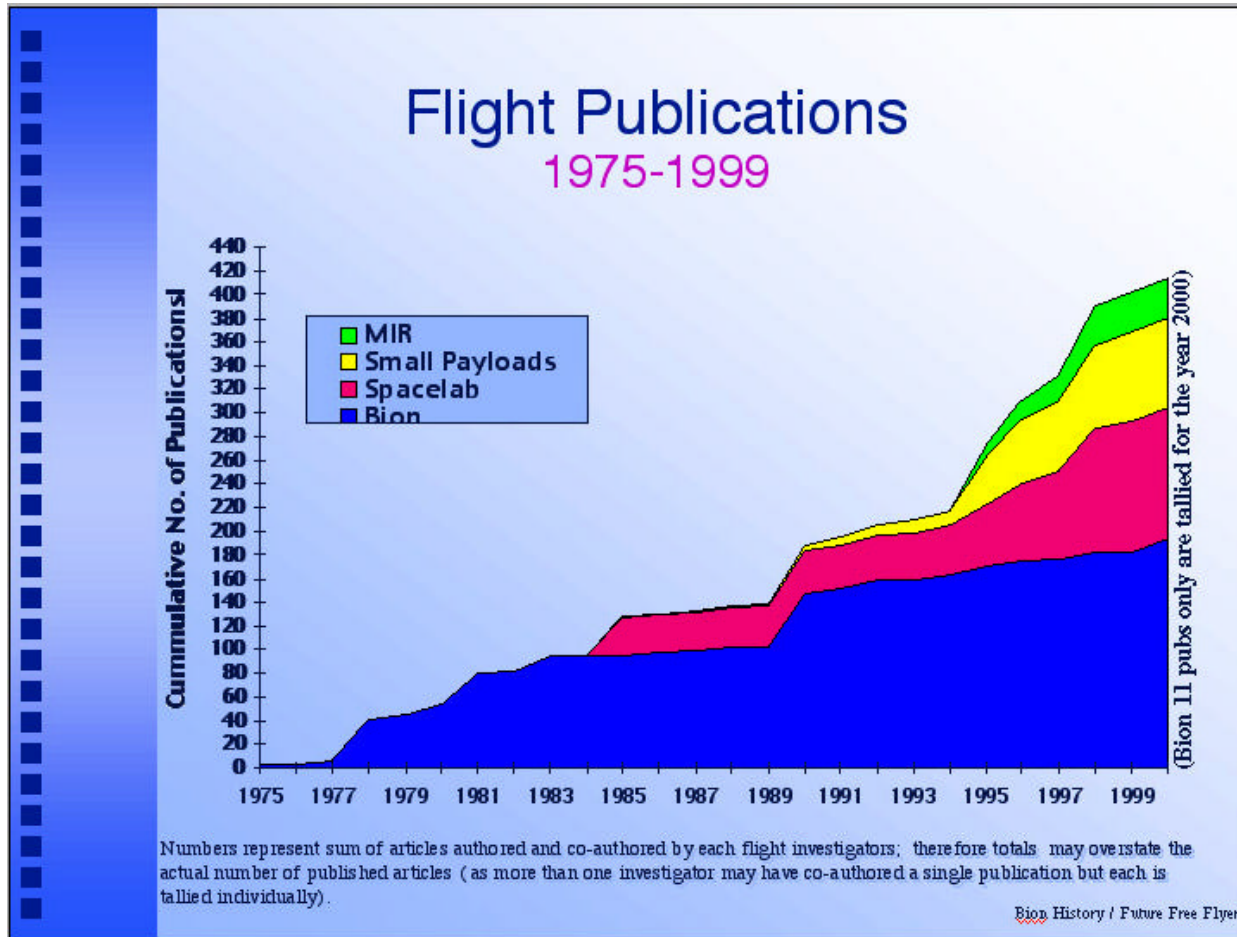


Figure 7. Summary of the number of payloads completed, in progress or planned, for each Research Program Office through Expedition 6.

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FSB: SMALL PAYLOADS PROJECT

- Backup Charts -- Science
 - Model Organisms
 - Generation Times
 - Data Gathering Strategy and Requirements
 - Organism vs. science vs. hardware strategy

FSB Science Goals

- Goal 1: Determine the gene-expression changes over time in a variety of individual model organisms exposed to the space environment.
- Goal 2: Determine if there are differences in DNA replication and repair processes in space, and what the long-term consequences might be.
- Goal 3: Determine changes in single nucleotide polymorphisms (SNPs) in large populations over multiple life cycles in the space environment.
- Goal 4: Determine the effects of the space environment on replication and reproduction over multiple life cycles.
- Goal 5: Determine how molecular processes within cells are altered in the space environment, and how the changes affect tissues, organs, physiological systems and whole organisms in space, throughout life cycles and multiple life cycles.
- Goal 6: Determine what phenomena observed during spaceflight are specific to gravity vs. other stresses (e.g. radiation).
- Goal 7: Determine the molecular causes of space medicine problems and other physiological changes caused by the space environment (e.g. bone loss, muscle atrophy, immune suppression, CNS effects, etc.).

Source: FSB Program Office submission to REMAP

Model Organisms*

What is a Model Organism?

- Research on a small number of organisms has played a pivotal role in advancing understanding in biology and medicine.
 - Many aspects of biology are similar in most or all organisms. A particular aspect is often easier to study in one organism versus others. The most studied organisms are called model organisms
 - The most popular model organisms have strong advantages for experimental research, such as rapid development with short life cycles, small adult size, ready availability, and tractability.
- Their value increases over time as more scientists add to the knowledge base.

NASA will contribute unique information on the nature of these pioneer organisms.

*The model organism pages were paraphrased from NIH's NCBI website:<http://www.ncbi.nlm.nih.gov/About/model/>

Model Organisms

Mammalian Models

- Mammals share many basic biologic functions, such as the regulation of cell division, development of organ systems, and immune response.
 - Mouse is the closest mammalian model organism to humans. The gene sequences that code for numerous proteins responsible for carrying out vital biological processes are very similar to humans. The mouse is a key system for studying and understanding human disease and for development new treatment strategies
 - Rat is the principal model organism to link function to genes. Rat models provide important strengths, often unique strengths, for human health and disease. The rat is the model of choice for cardiac and vascular function, pulmonary circulation, metabolism, neurological control, age and gender related differences, studies related to hypertension and signal transduction.

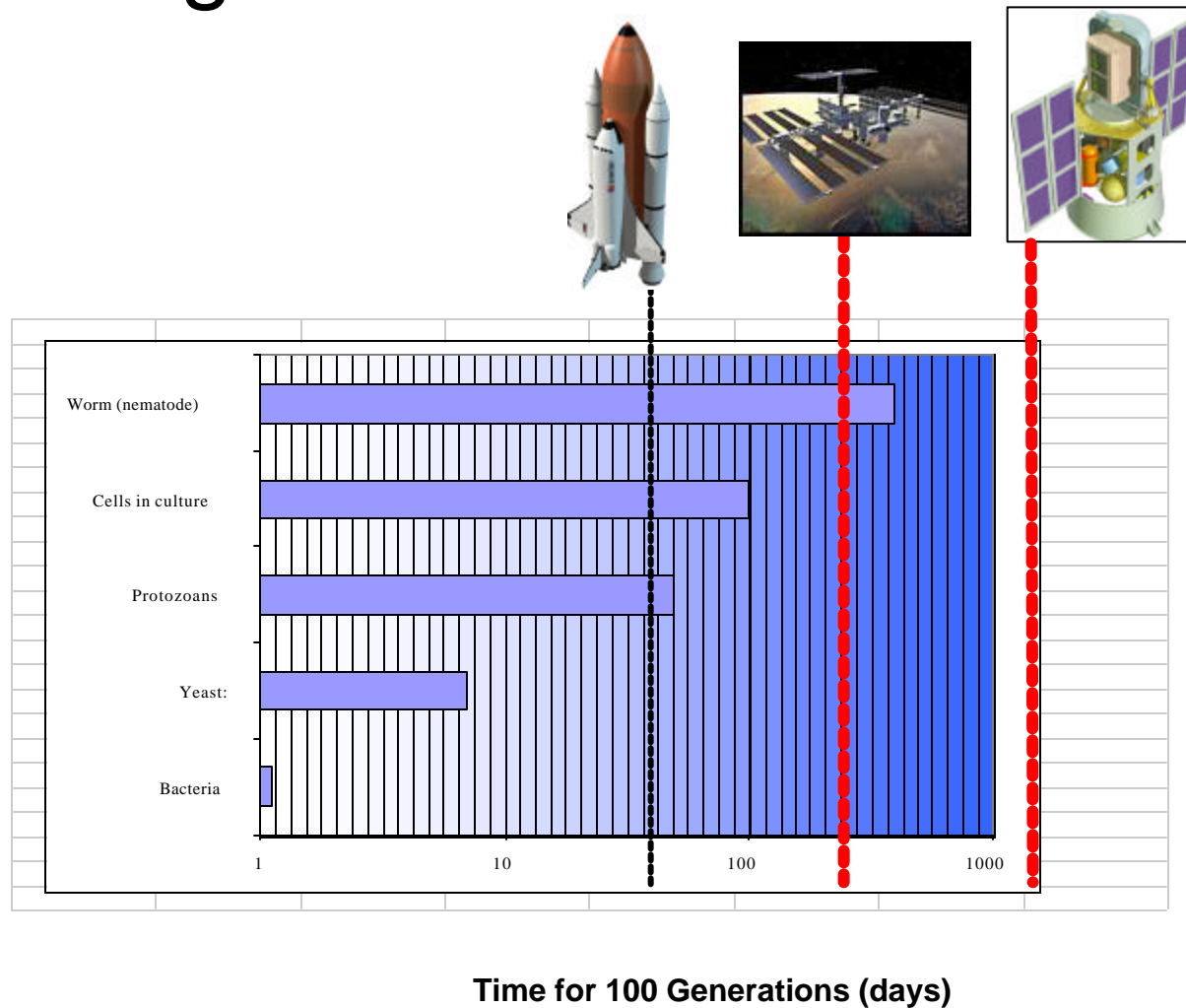
Model Organisms

Non-Mammalian Models

Each model described below has advantages for the study of certain mammalian biological processes and has been a pioneer in developing the fields of cell and molecular biology.

- Microbes - have solved many problems in agriculture, disease prevention, industrial processes, and medicine.
- Fruitfly (*Drosophila*) has an easy to manipulate genetic system. Its biological complexity is comparable to a mammal and many gene functions are very similar to those in mammals. *Drosophila* provided new insights into cancer, neurodegenerative diseases, behavior, immunity, and aging..
- Roundworm (*C. elegans*) is the best characterized multicellular animal for genomics, genetics, embryology, and cell and neurobiology. It is unique in that it can be grown and genetically manipulated with the speed and ease of a micro-organism, while offering the features of a real animal. *C. elegans* has a full set of organ systems, has complex sensory systems, shows coordinated behavior. It is further distinguished by the ability to trace the lineage of every one of its 1000 constituent cells. In addition, the morphology, development and function of each of its cells has been mapped in great detail.
- Yeast (*S. cerevisiae*) is used as a reference for extracting the sequences of human and other higher eukaryotic genes. Ease of genetic manipulation allows for conveniently analyzing and functionally dissecting gene products from other eukaryotes.
- Arabidopsis is the organism of choice for basic studies of plants because of its small genome and ease of growth and manipulation. Applications include agriculture, energy, environment, and human health.

Multigenerational studies



Data Gathering Strategy for Biological Reference Standards

Bacteria, yeasts, *Drosophila*, *C. elegans*, plants, fish
Human and animal tissue cultures
Cell lines
Embryos
Eventually human and mammal subjects

Time course, cell cycles, life cycles, *n* generations

Research platforms	Space ⇒	Δ organism/ environment interface	Signal ⇒	Δ gene expression	mRNA ⇒	Δ protein complement	⇒	Δ metabolism	Δ structure
Shuttle Cells, tissues, adaptation	Start experiment in space via freezing, dormancy adding nutrients in flight	- gravity - shear - density-driven forces - coriolis - turbulence - convection + radiation measured with sensors	Cell senses change and transcription proteins migrate to nucleus to turn on gene expression Measure via <u>proteomics</u>	Analyze whole genome microarray	Fix + refrigerate or Freeze @ (-80°C) Enables cDNA library	Freeze -20°C Snap freeze @ (-80°C), store @ (-120°C) ----- fluorescent proteins ----- analyses scale with available sample ----- correlate with gene array data		Substrates for different enzymes ----- Time samples	Fix for electron, <u>confocal</u> , other microscopy
Early ISS Small organisms, life cycles, tissue aggregates				Use species where whole genome is known					
Later ISS Larger organisms, multiple generations, evolution				leverage and contribute to databases					
Planets									

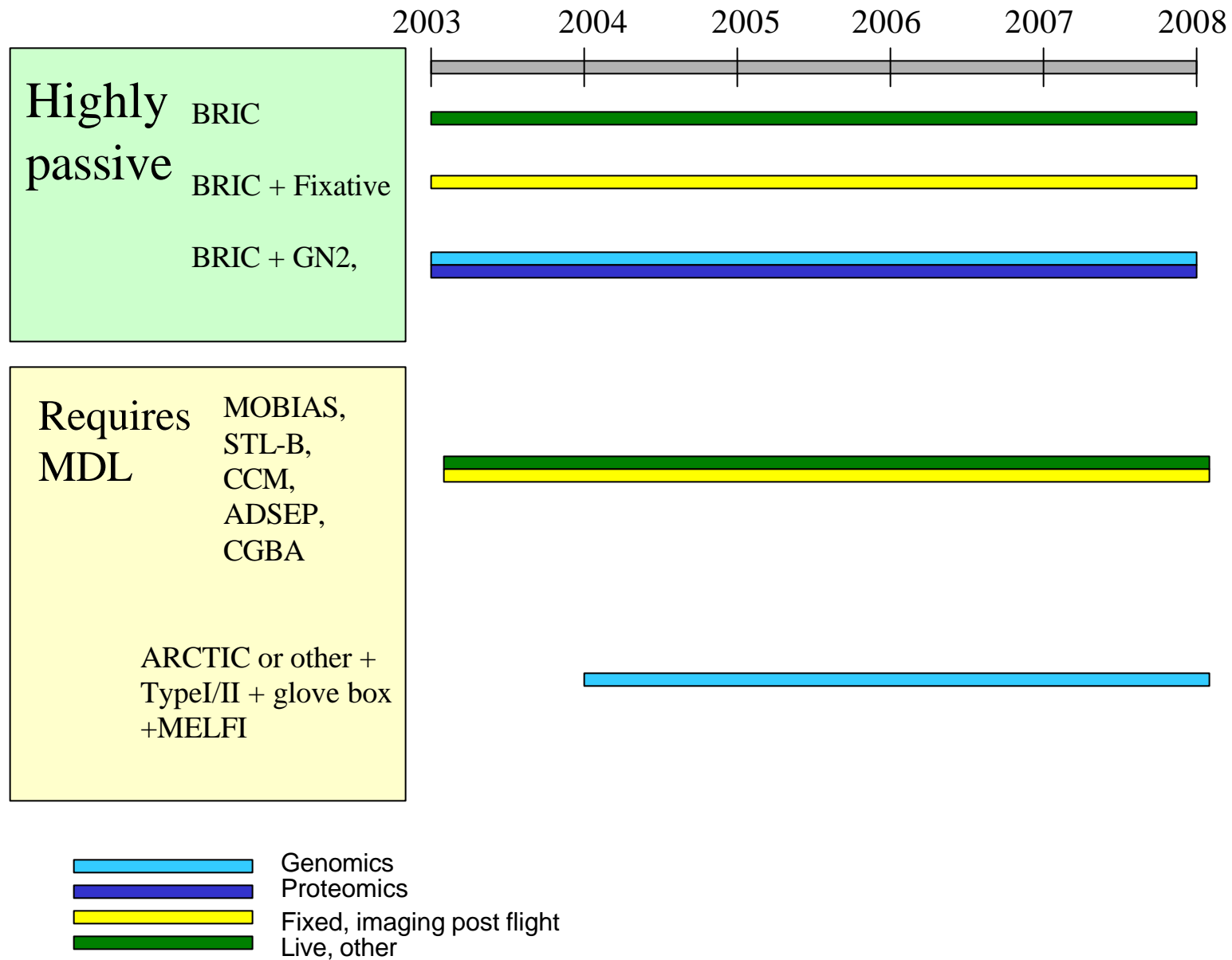
FSB: Small Payloads Project

Experiment Examples

	<i>C. elegans</i> Precursor	<i>C. elegans</i> Radiation	<i>Arabidopsis</i> Radiation	Bacteria
Objectives	OptiCell performance Growth and development Egg laying rate Gene expression Signal transduction Radiation sensitivity Behavior	Gene expression Radiation sensitivity	Test novel approach Gene expression Radiation sensitivity	Gene expression Radiation sensitivity
Specimen	Adults	Dauer larvae	Imbibed seeds	TBD
Temperature at launch	6 °C	Ambient	Ambient	-195 °C
Temperature on orbit	25 °C	Ambient or controlled	Ambient or controlled	37 °C
Temperature at landing	-195 °C	-195 °C	Ambient or -195 °C	-195 °C
Facility hardware	BRIC 60 GN ₂ Freezer JPL Video system PTCU* Temperature recorder Soft storage locker	BRIC 60 GN ₂ Freezer PTCU* Temperature recorder	BRIC GN ₂ Freezer? PTCU* Temperature recorder	ADSEP, CGBA GN ₂ Freezer PTCU* Temperature recorder
Experiment hardware	modified OptiCell	modified OptiCell	TBD	TBD
Expt. duration (days)	45 +	15 +	15 +	15 +

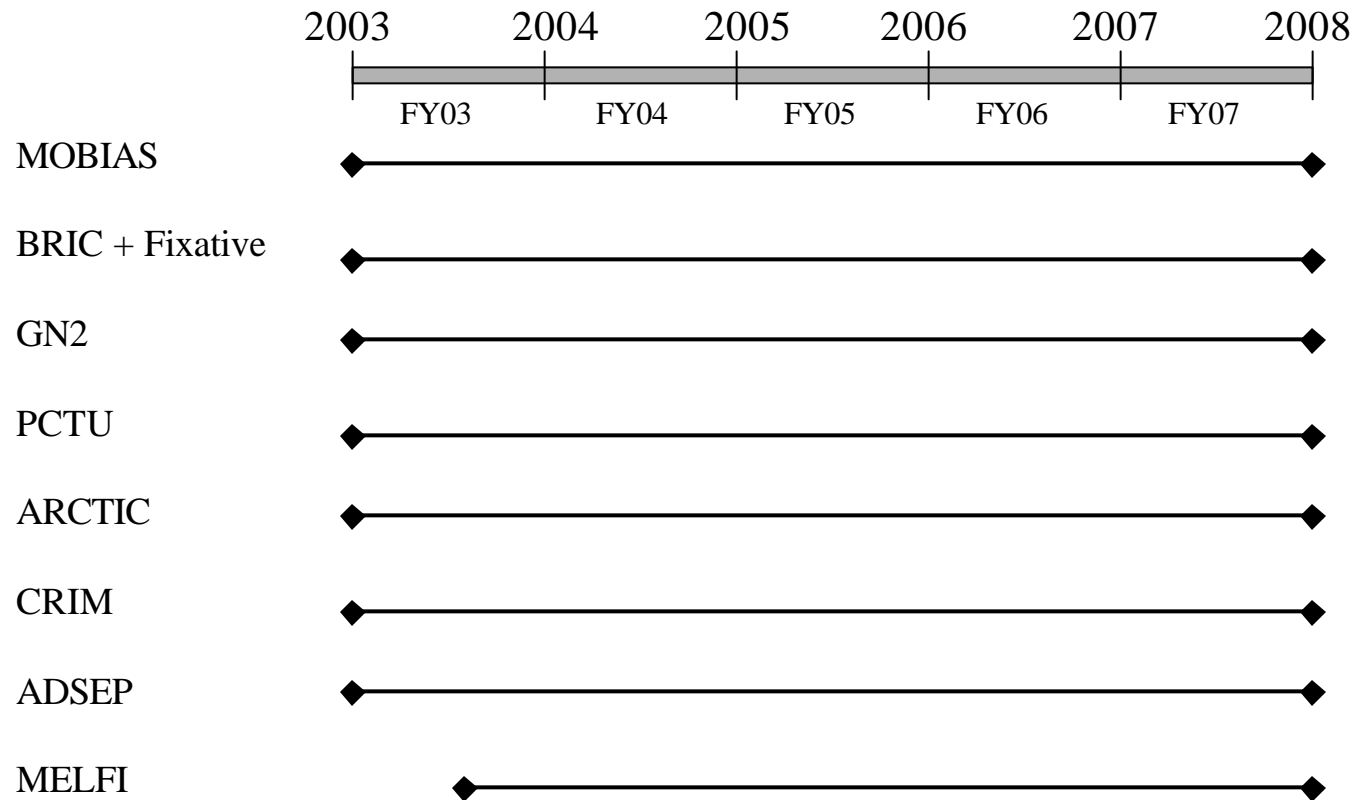
*PTCU = ESA's Passive Thermal Control Unit

Potential yeast experiment flights and type of science returned:

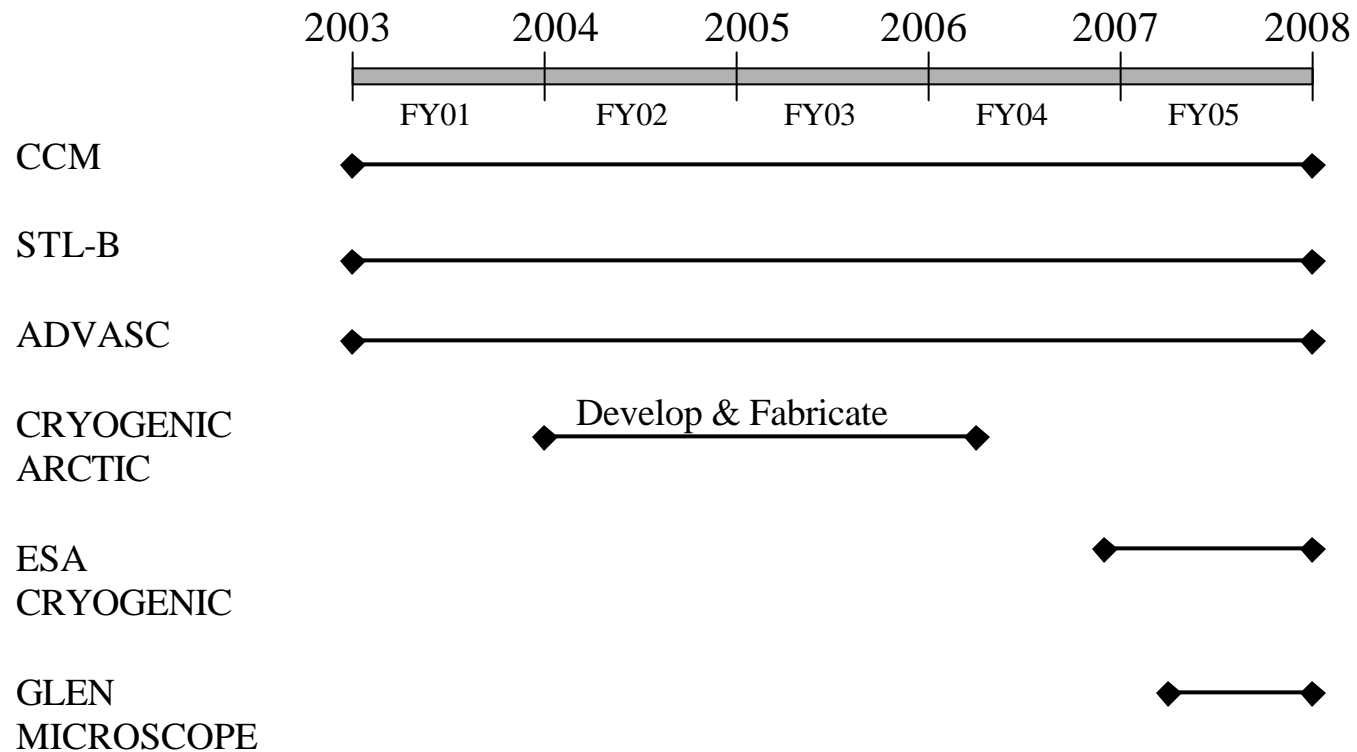


**FSB: SMALL PAYLOADS PROJECT
FLIGHT HARDWARE AVAILABLE NOW**

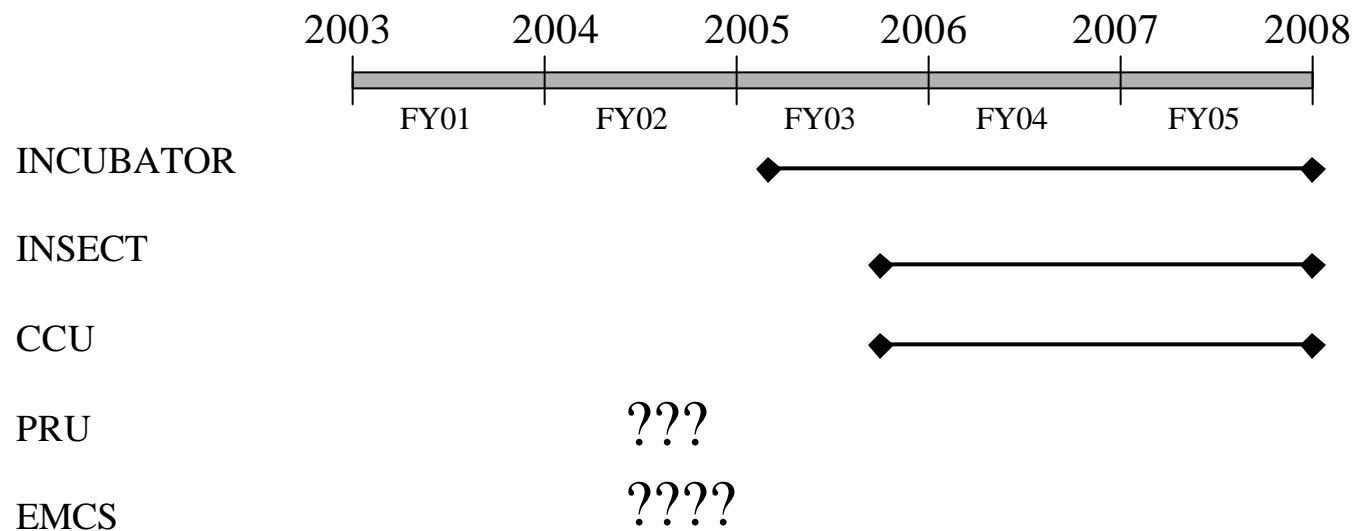
- OPPORTUNITIES
- Hardware available for flight



- Opportunities
 - Hardware available for flight



- Fundamental Space Biology Small Payloads Opportunities
 - Hardware available for flight



Fundamental Space Biology Small Payloads Plan

- DISCUSSION OF IMPLEMENTATION OPTIONS

Implementation: Discussion

- Dear colleague letter - Detail the constraints of the hardware and flight, solicit the best, most creative, highest science return experiments - *trust the creativity of the scientists to work within these constraints*
- Streamline the process by which experiments from this response are chosen - *perhaps by*
 - Assign choice to NASA scientists
 - Appoint a small SWG to meet annually for each years selection, *or*
 - Use current peer reviewed process
- Data archiving/Bioinformatics program – essential to preserve information for the future and to allow data mining throughout lifetime of program.